Spatial modeling in support of measles control and elimination

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Global Health, Bill & Melinda Gates Foundation

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The contribution of models

Program questions

- Where are gaps in routine MCV coverage?
- Where are there unvaccinated persons? Where are the remaining susceptibles?
- Where is there likelihood of transmission?
- What is the relative importance of doses received via RI and SIAs?
- How can SIA effectiveness be measured? How do we best plan SIAs?
- How effective is outbreak response vaccination?

Cutts et al. (2020)

But how do we get there?

Program questions

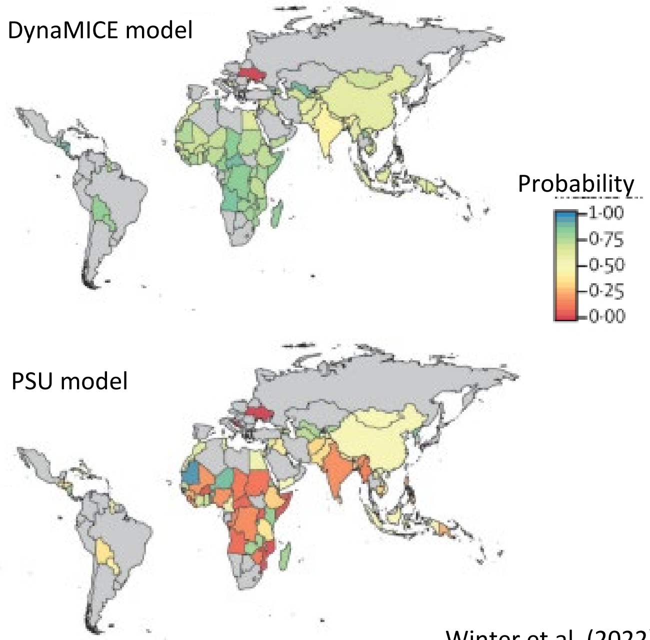
VS

Program benchmark

Existing benchmarking for measles elimination focuses on threshold coverage targets or “snapshot” scenarios

- Vaccine coverage targets*:
  95% MCV1 and MCV2 at national or district level
- Surveillance targets*:
  ≥2 suspected cases per 100 000 population discarded as non-measles and non-rubella
- Regional goals:
  6 WHO regions

Probability of measles elimination by 2050 with intensified investments



*not elimination specific

Winter et al. (2022)

Historical examples demonstrate that high levels of MCV coverage is neither necessary or sufficient for elimination

Category	Number of Countries	MCV1 >95%	MCV1 <95%
Verified	82	28 (34%)	54 (66%)
Eliminated	21	5 (24%)	16 (76%)
Endemic	85	16 (19%)	69 (81%)
Re-established endemic transmission post-verification	5	2 (40%)	3 (60%)
No report	1	1 (100%)	0 (0%)

Data source: Regional Verification Reports; Crowcroft et al. (2024)

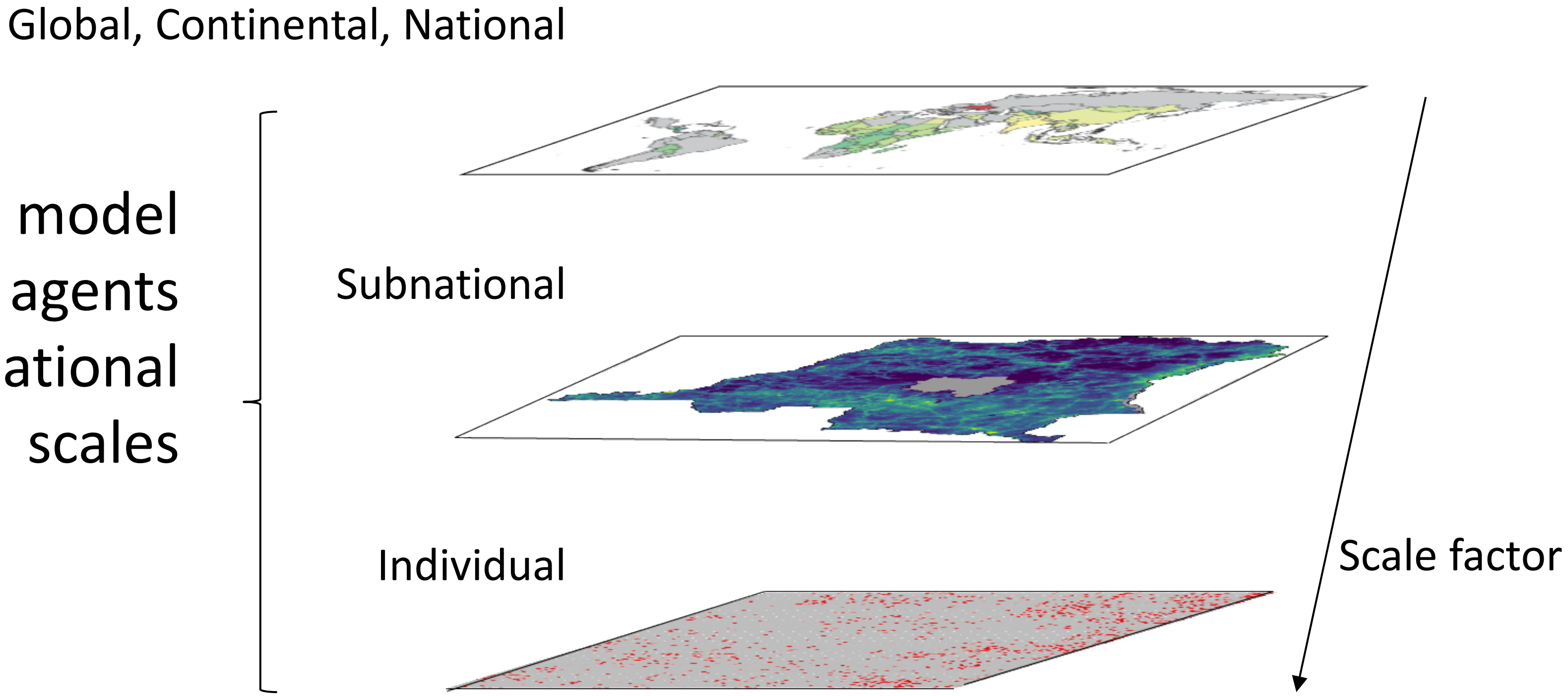
How can modeling provide better performance metrics to drive and assess programmatic decisions?

Outline

- Motivation
- Model and Calibration
- Spatial coverage distributions
- Conclusion

We require high spatial and individual resolution

We want to model individual agents on multi-national scales



Figures from Winter et al (2022), Cheng et al (2021), and Truelove et al. (2019)

Leveraging software and hardware designs 🚀

- Properties as arrays
- “Just the properties” philosophy
- Reducing reporting
- Deterministic demographics
- Cohorts(ish)
- New(ish) algorithms
- Interpreted, dynamically types languages (e.g., python) + JIT

agents

0: age, vax, home | 1: age, vax, home | 2: age, vax, home

[… more agents …]

N: age, vax, home

VS

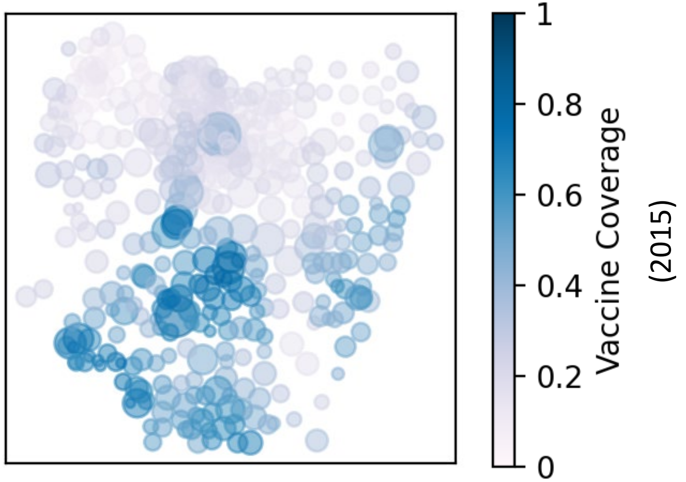
properties

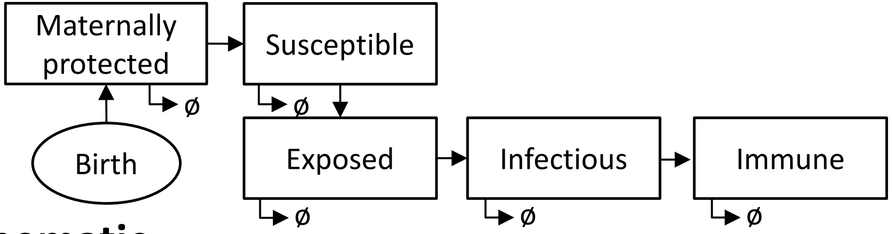
age_0	age_1	[…more agents…]	age_N
$home_0$	$home_1$	[…more agents…]	$home_N$
vax_0	vax_1	[…more agents…]	vax_N

We build a high spatial resolution model using a python framework for agent based spatial disease models (LASER)

- Northern Nigeria Scenario (Admin 2)
  - Vaccine coverage
  - Demographics (population and vital dynamics)
- Scenario used for calibration
- Agent based, metapopulation model written in python with acceleration via numpy and numba
- 419 nodes, 96M initial agents
- Gravity model

Northern Nigeria Map





Disease state schematic

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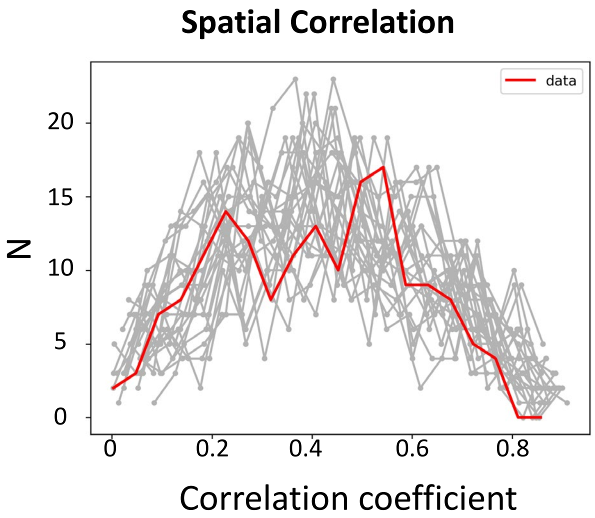
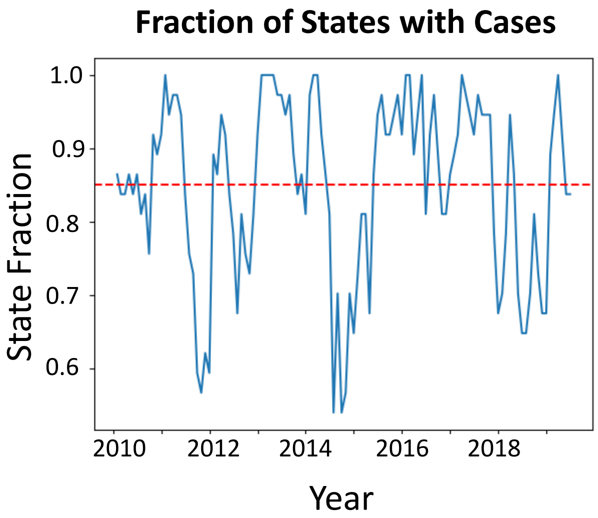
We calibrate against spatio-temporal data from Northern Nigeria spanning 2010 to 2020





Potential other data sources for calibration:

- Historical case data
- Seasonality
- Case age distribution
- Serology surveys
- Travel data
- Night lights
- …

Limitations:

- Under-reporting
- Heteroskedasticity
- Impact of SIAs
- Uncertainty in inputs/initial conditions (e.g., demographics)
- Applicability to future scenarios

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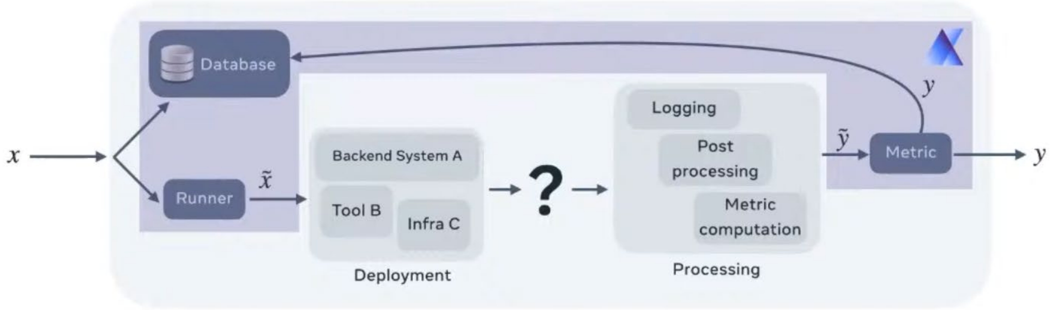
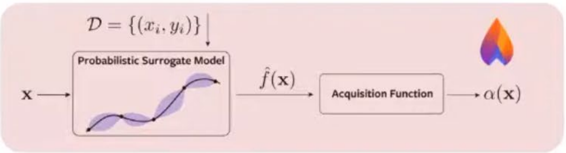
We leverage an adaptive experimentation platform to calibrate this noisy, multi-objective problem

Ax is an accessible, general-purpose platform for understanding, managing, deploying, and automating adaptive experiments.

- Versatile
- Customizable
- Production-complete
- Multi-modality and constraints
- High-noise settings
- Easy to use

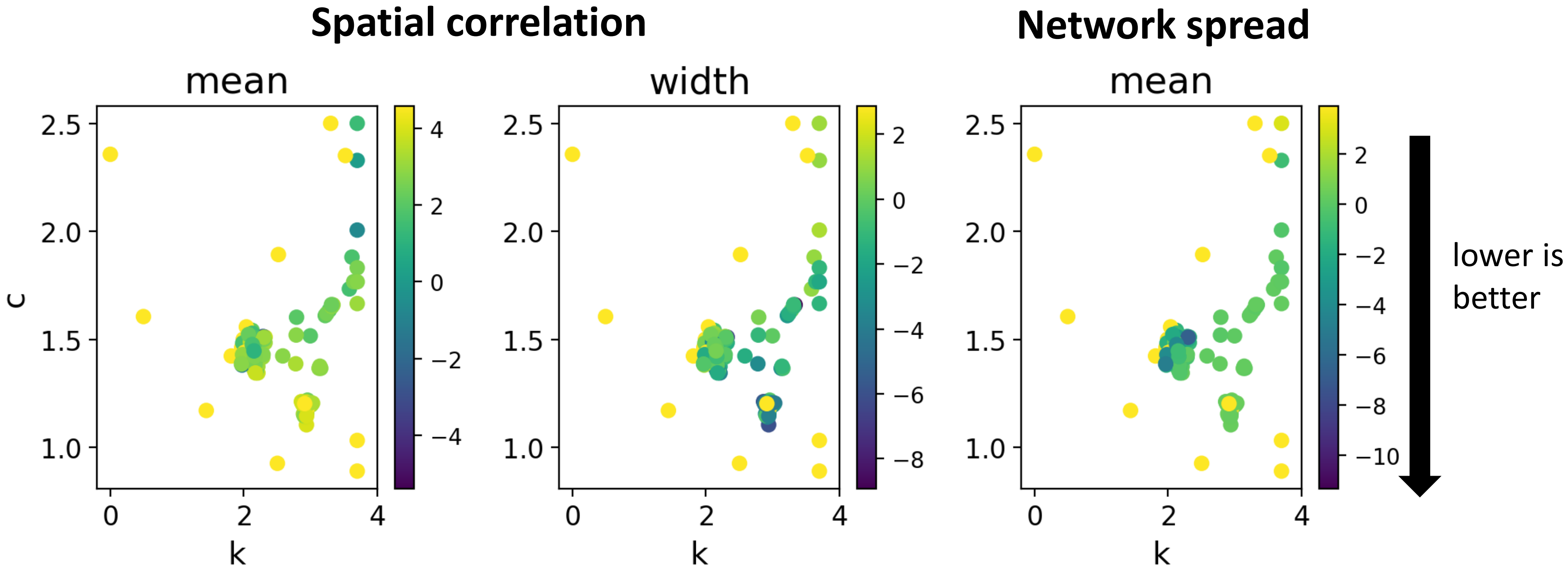
Ax + BoTorch conceptual framework





Balandat et al. (2020)

Multi-objective calibration of gravity model parameters



126 samples using the ax+botorch "out of the box"

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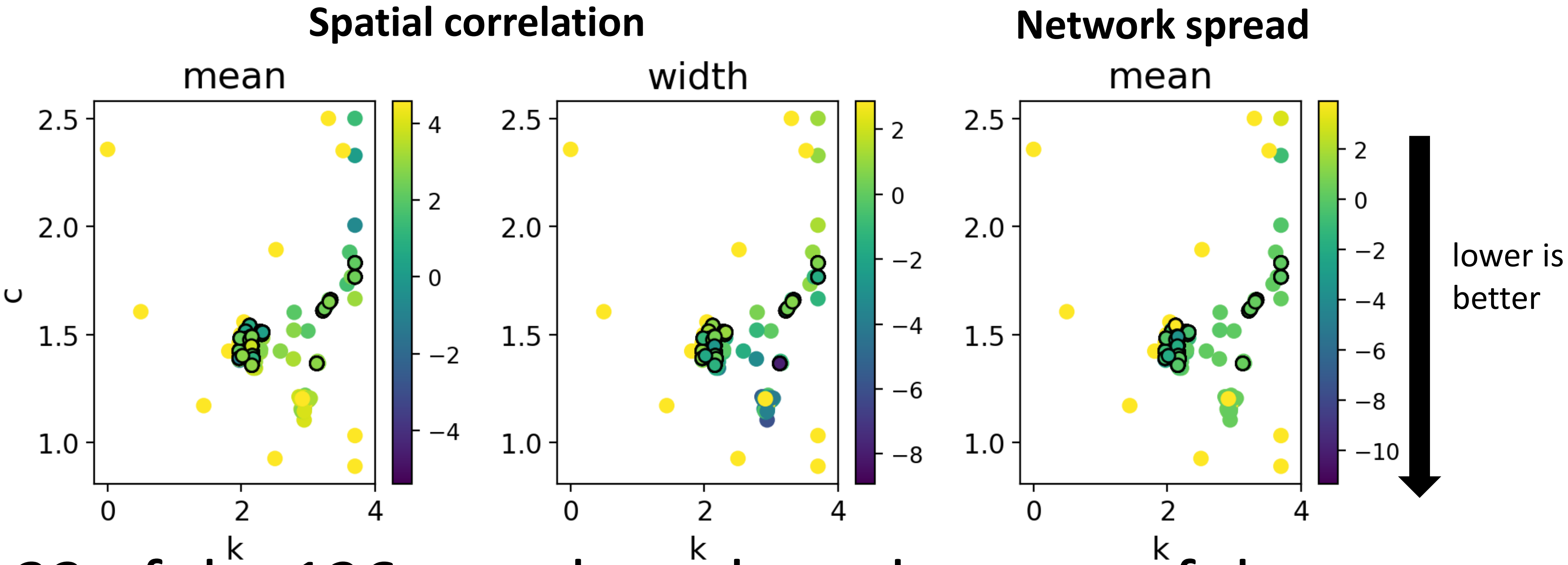
Multi-objective calibration of gravity model parameters define a pareto-front



33 of the 126 samples selected as part of the pareto front

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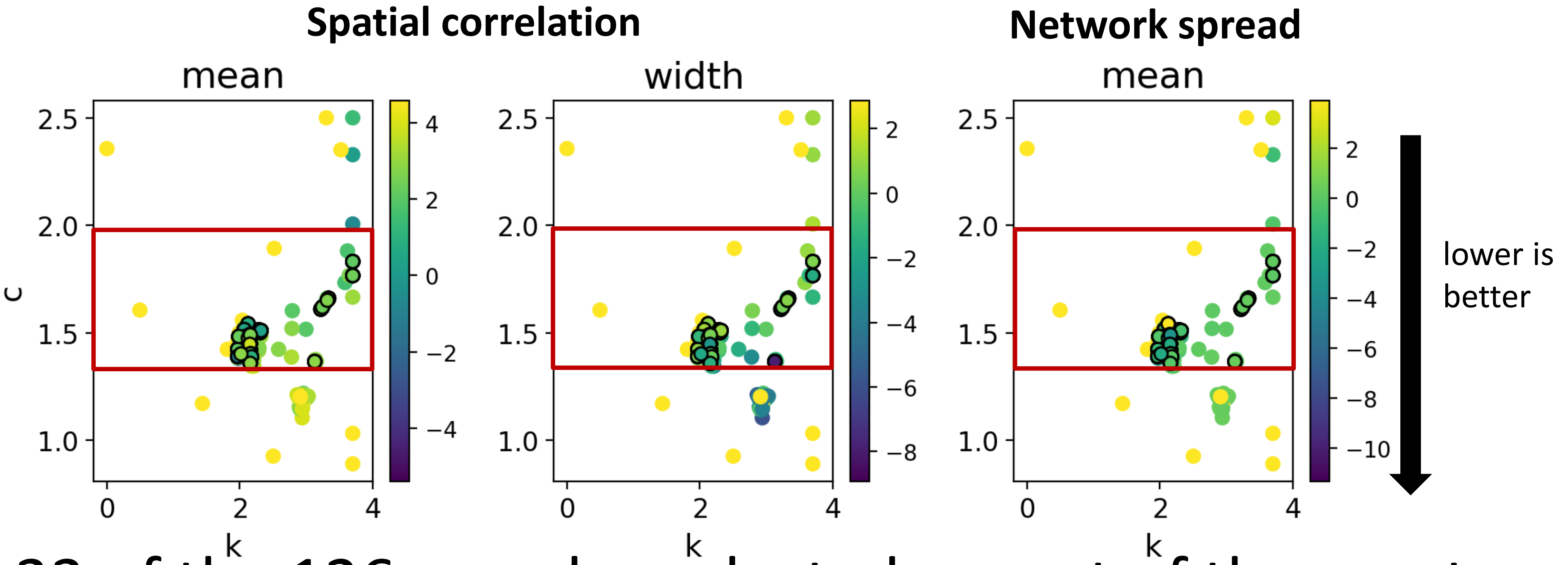

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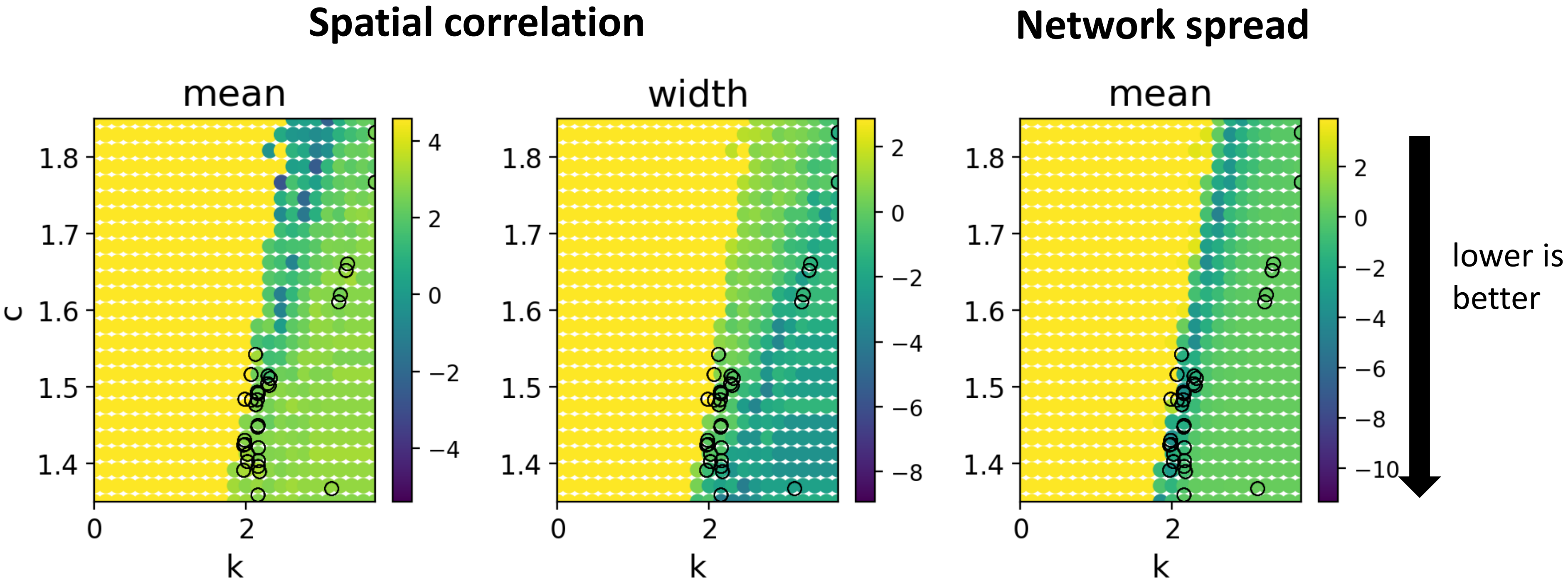
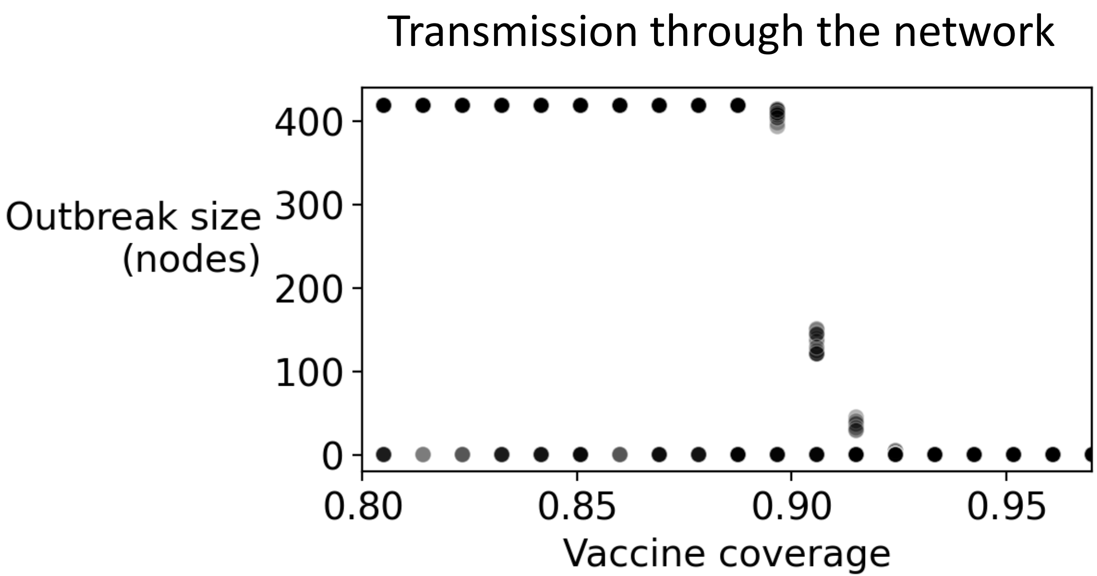


6250 simulation grid search

We look at transmission through the network as a metric of how local outbreaks might threaten elimination status



- Uniform vaccine coverage ranging from 75% to 97%
- Seed network with a single infected individual
- Plot number of nodes with an outbreak after 4 years
- N = 25 random seed samples per vaccine coverage level

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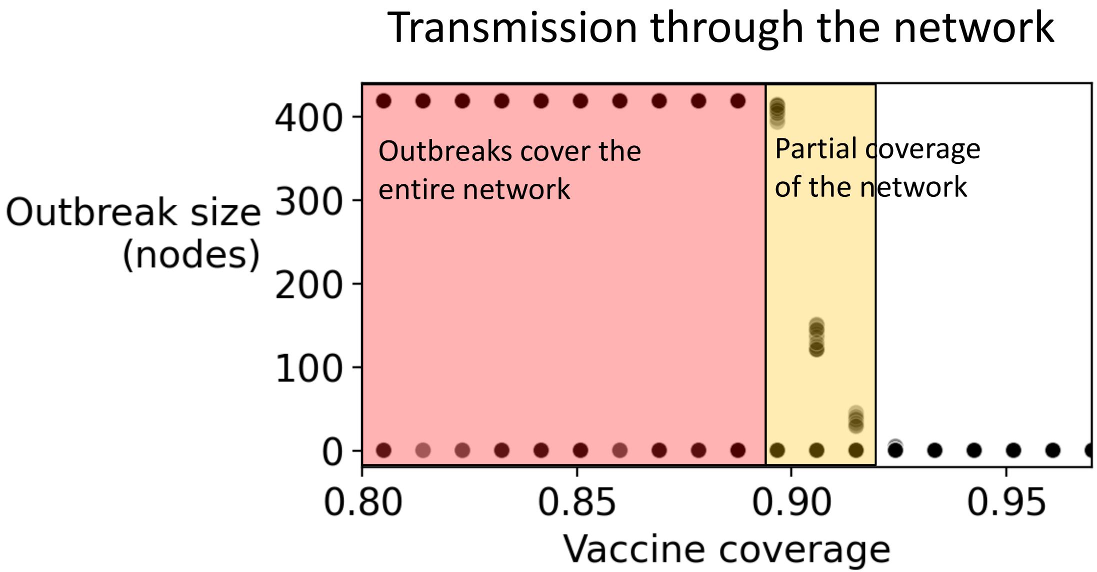

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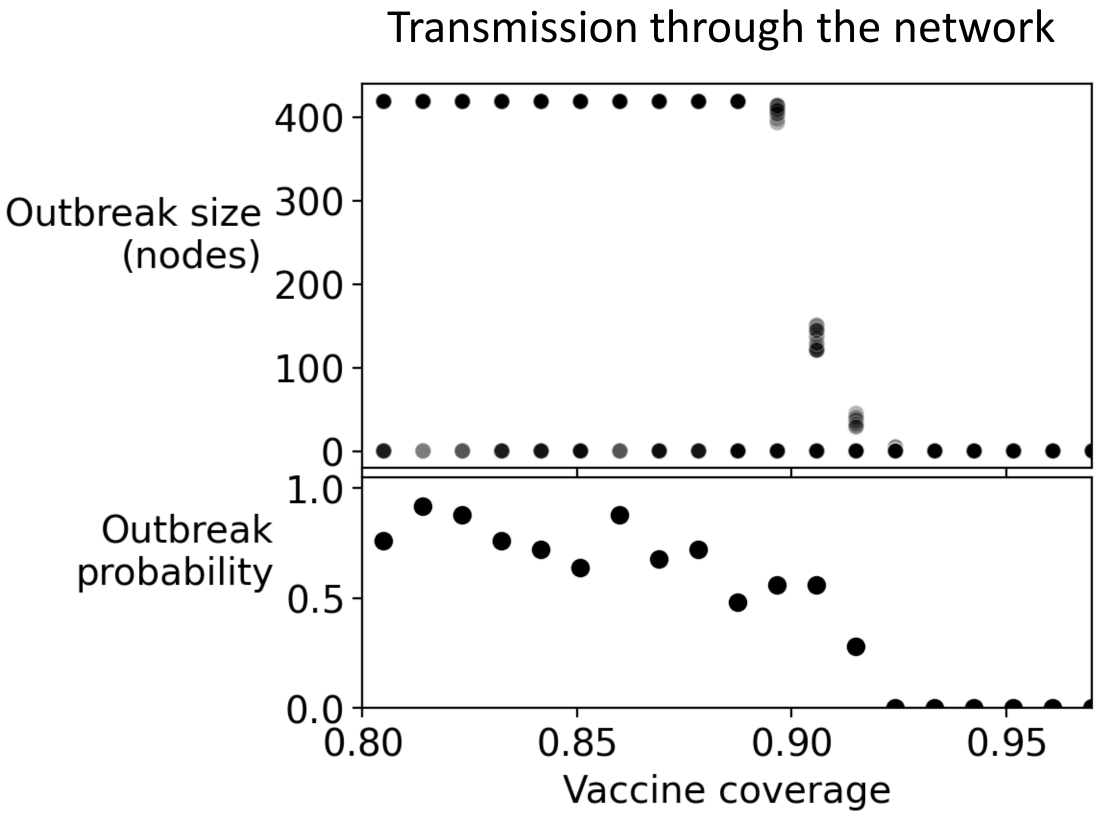

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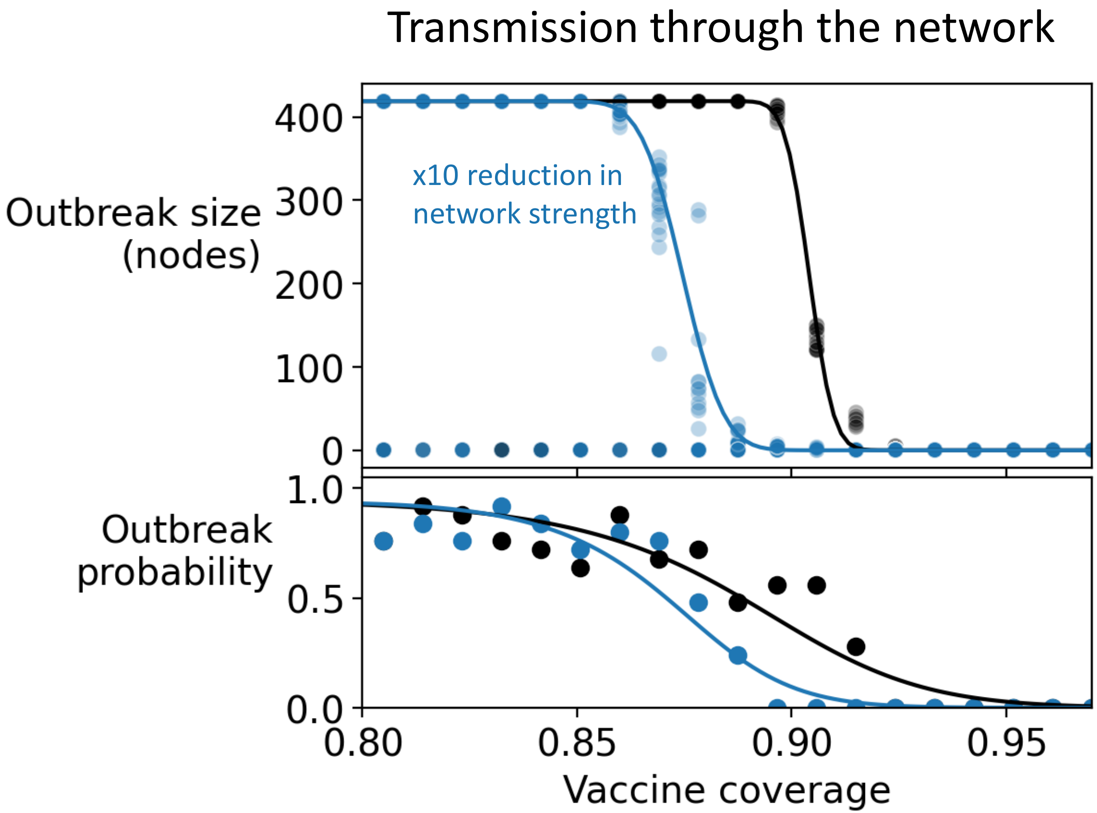

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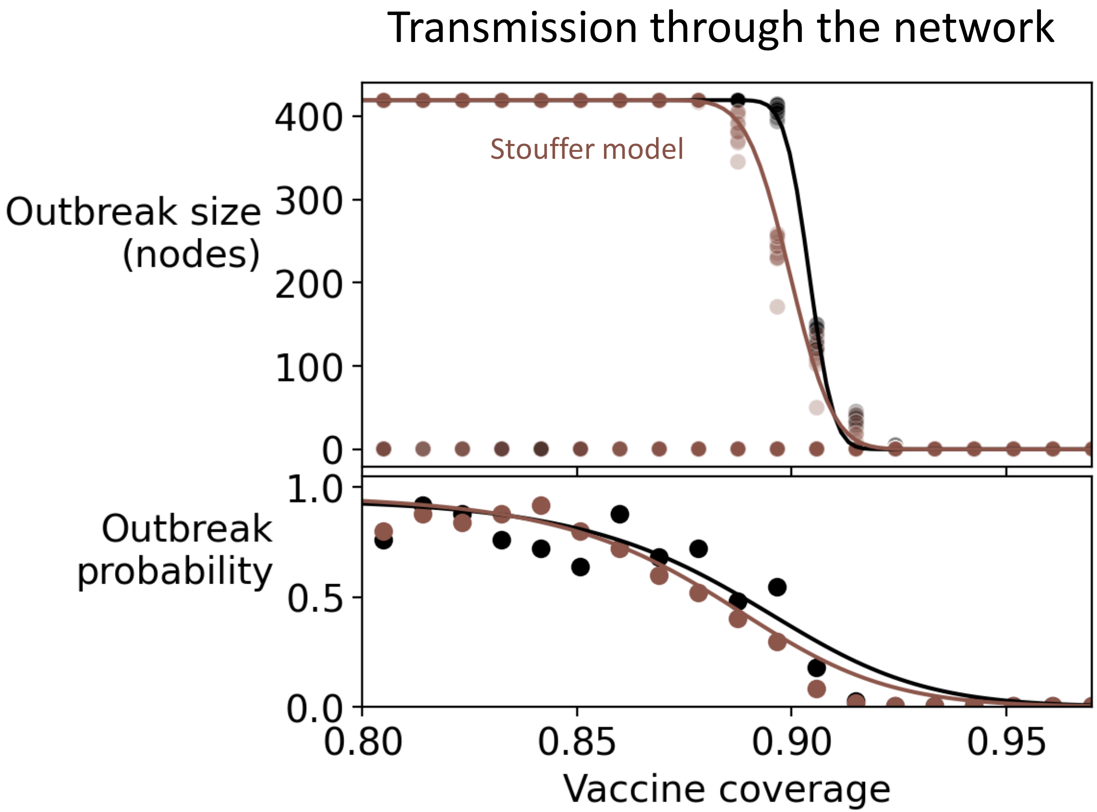
We are also looking at other spatial network designs



- Uniform vaccine coverage ranging from 75% to 97%
- Seed network with a single infected individual
- Plot number of nodes with an outbreak after 4 years
- Compare gravity to Stouffer model: outbreak probability similar, but extent may be different
- How can we motivate our choices?

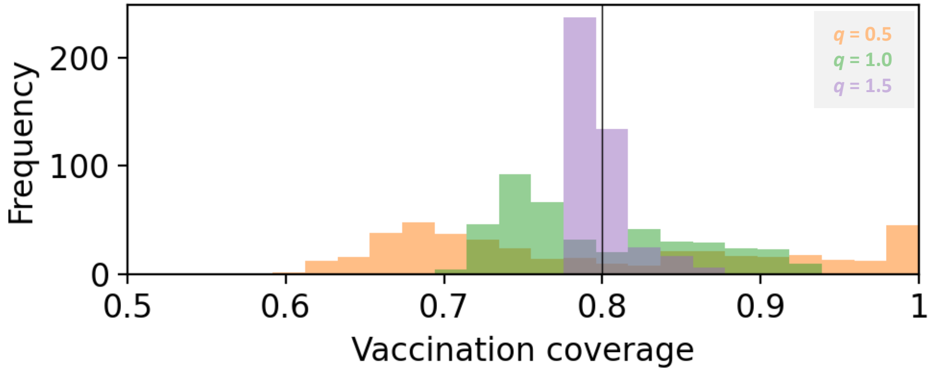
We use existing vaccination maps to build distributions with a target coverage

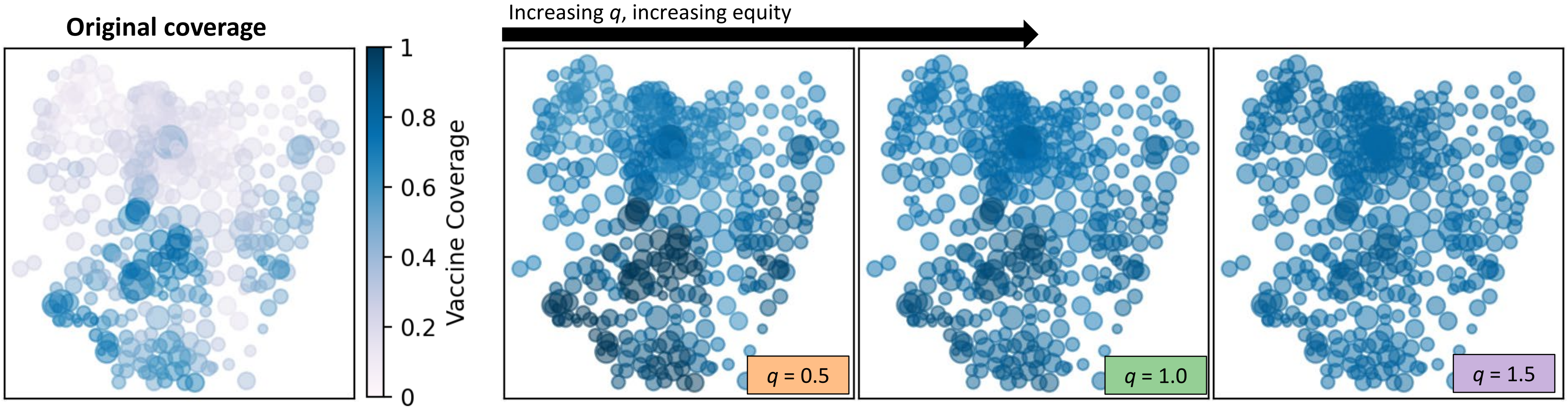
Scale initial Northern Nigeria node vaccine coverage ($V_i(0)$; below) to total target coverage $V_N(t)$:

$$V_i(t) = V_i(0) - \left(\frac{V_N(0) - V_N(t)}{\sum_{j=0}^{N} p_j V_j^q(0)}\right) V_i^q(0)$$

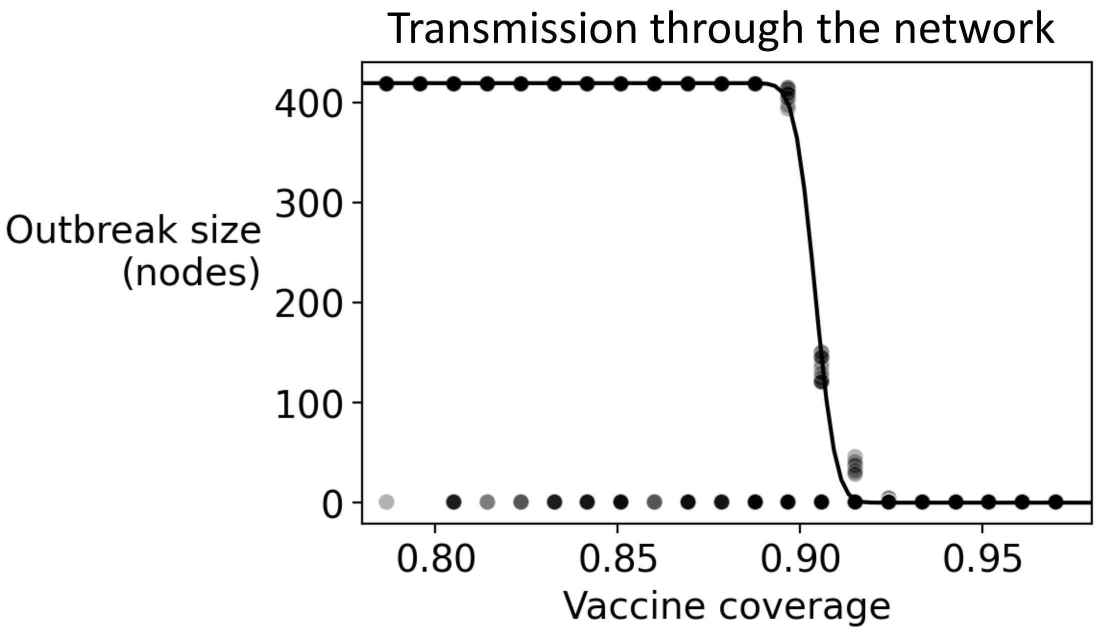
q is our equity factor where increasing q corresponds to increasing equity.

Winter et al. (2022)





We construct “pattern based” vaccine coverage distributions to investigate impact of vaccine equity



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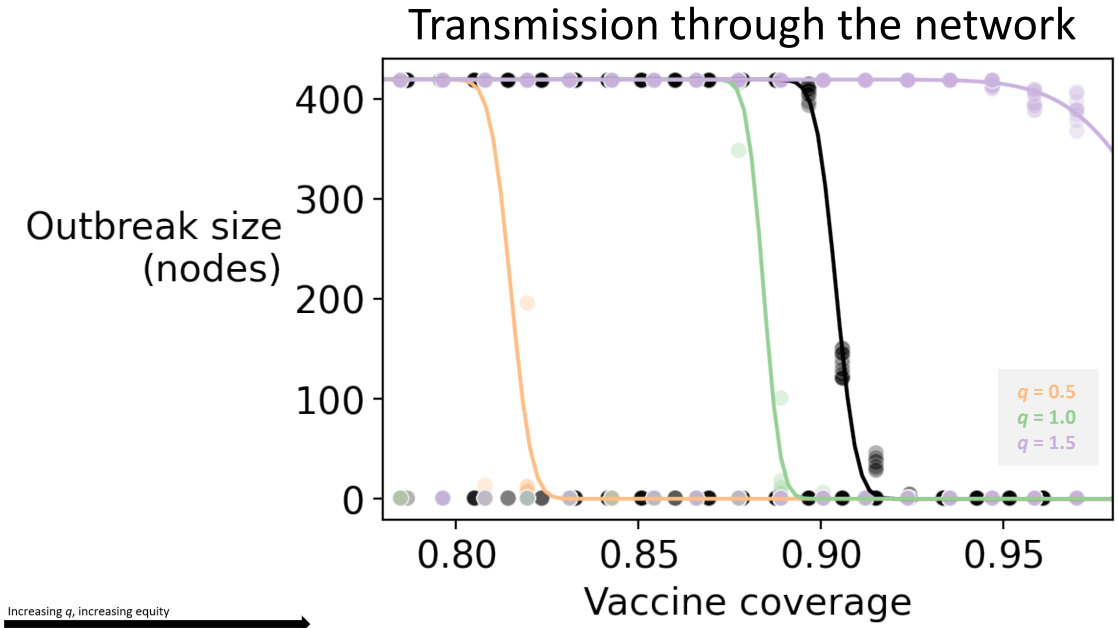

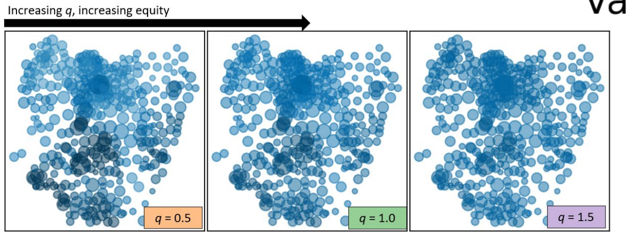

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- Seed network with a single infected individual
- Plot number of nodes with an outbreak after 4 years
- N = 25 random seed samples per vaccine coverage level
- Introducing spatial structure to RI coverage sees fewer outbreaks in least equitable scenario – why?

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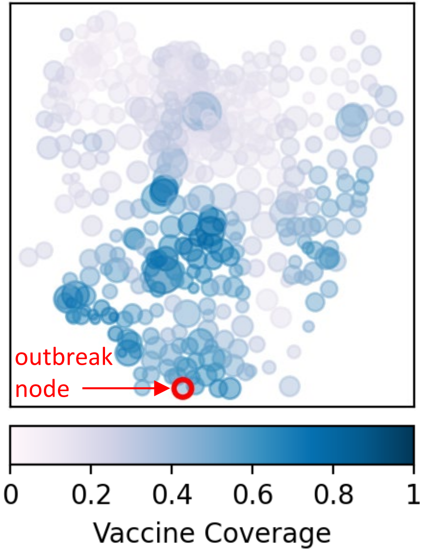
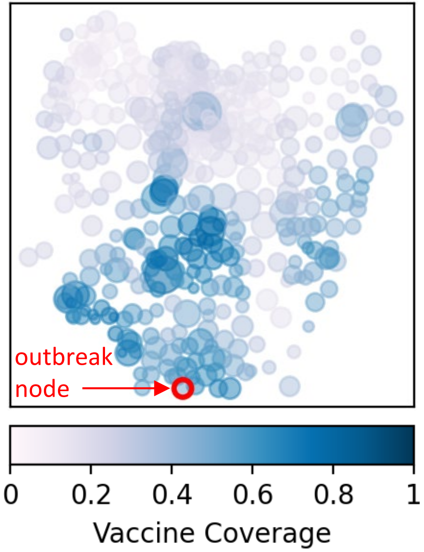
A closer look at the importation and distribution conditions highlights their importance

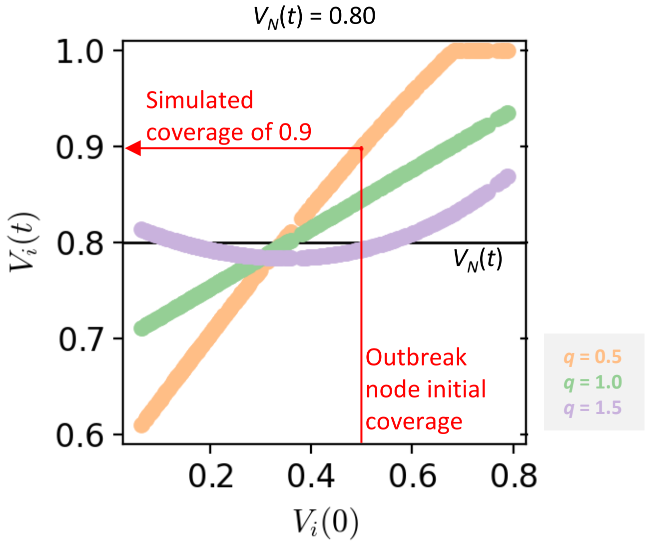


- Seeding in single node with relatively high initial coverage means that low *q* favors that node

A closer look at the importation and distribution conditions highlights their importance

Parameterized coverage versus input (data) coverage





- Seeding in single node with relatively high initial coverage means that low q favors that node
- Coverage parameterization leaves many nodes below target $V_N(t)$ for high q
- What are alternative importation schemes?

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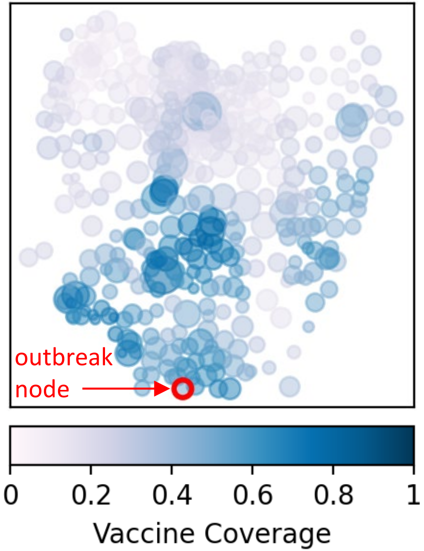

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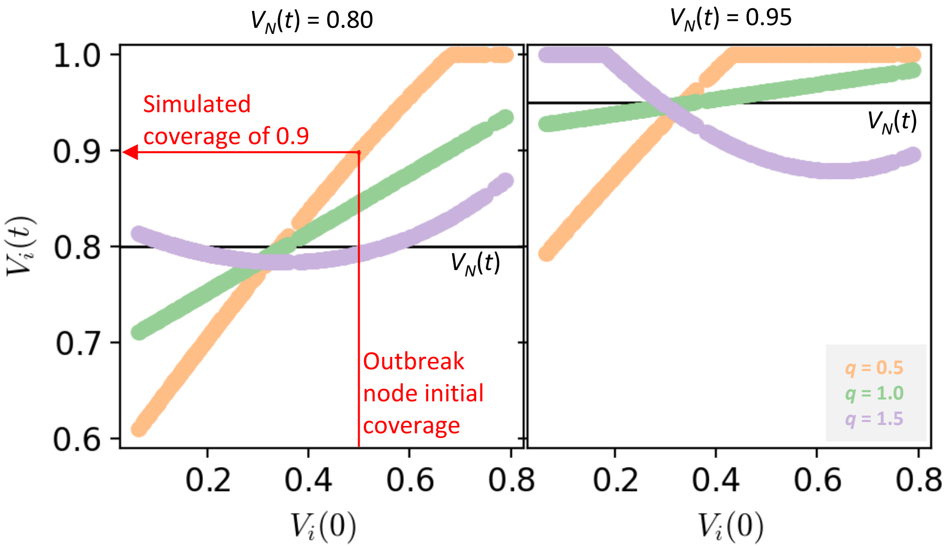

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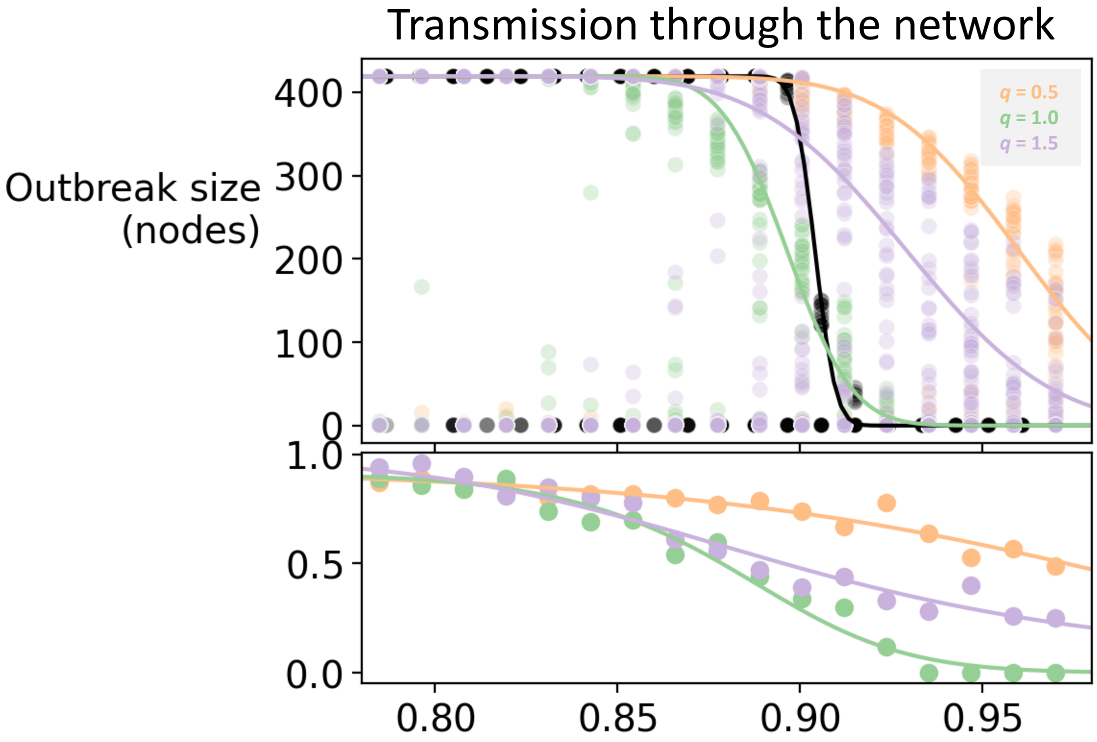
Weight importation event by zero dose population now has least equitable scenario trending towards outbreaks



- Uniform vaccine coverage ranging from 75% to 97%
- Seed network with a single infected individual
- Plot number of nodes with an outbreak after 4 years
- N = 100 random seed samples per vaccine coverage level

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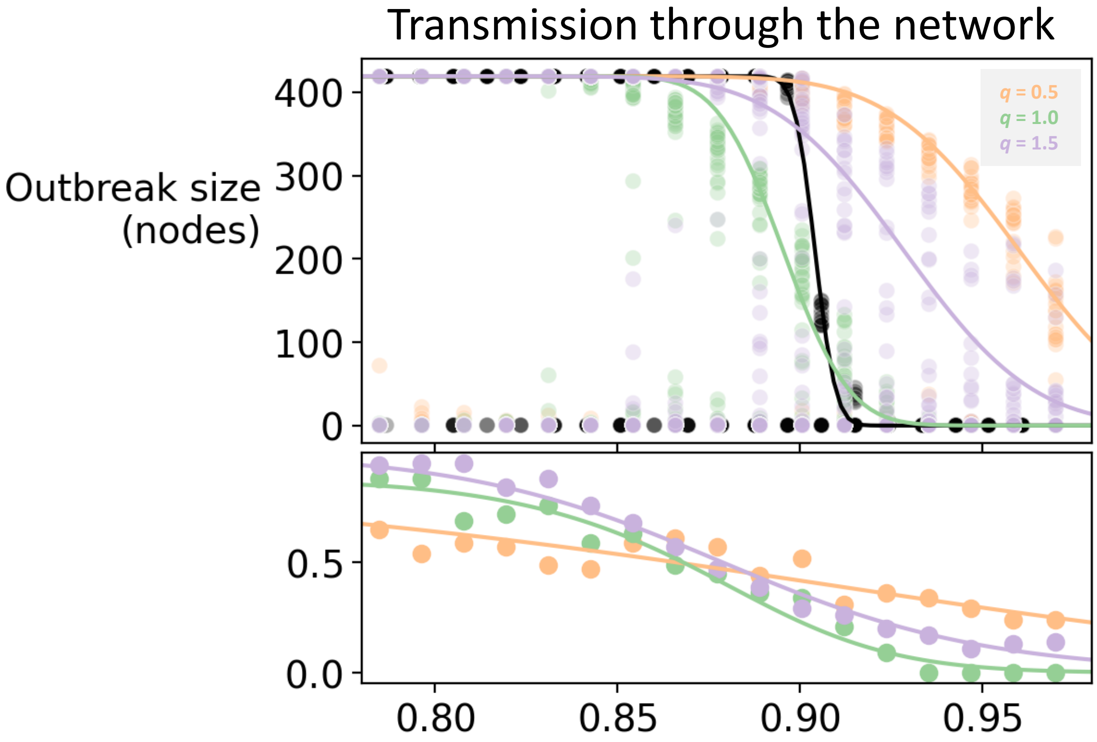
Weight importation event by population is quite similar to zero dose scenario



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- Plot number of nodes with an outbreak after 4 years
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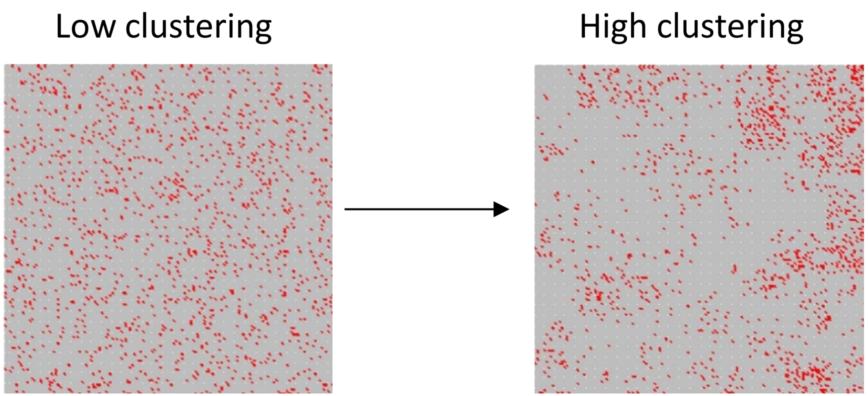
Conclusion

- Clear need for new tools and thinking towards measles elimination
- Opportunity for additional benchmarking
- Thinking beyond national and subnational coverage:
  - Connectivity/network models
  - Importation risk
  - Equity and coverage patterns
- Opportunity areas:
  - Inputs and projects for initial conditions (e.g., demographics, connectivity, mobility models)
  - Model calibration and validation

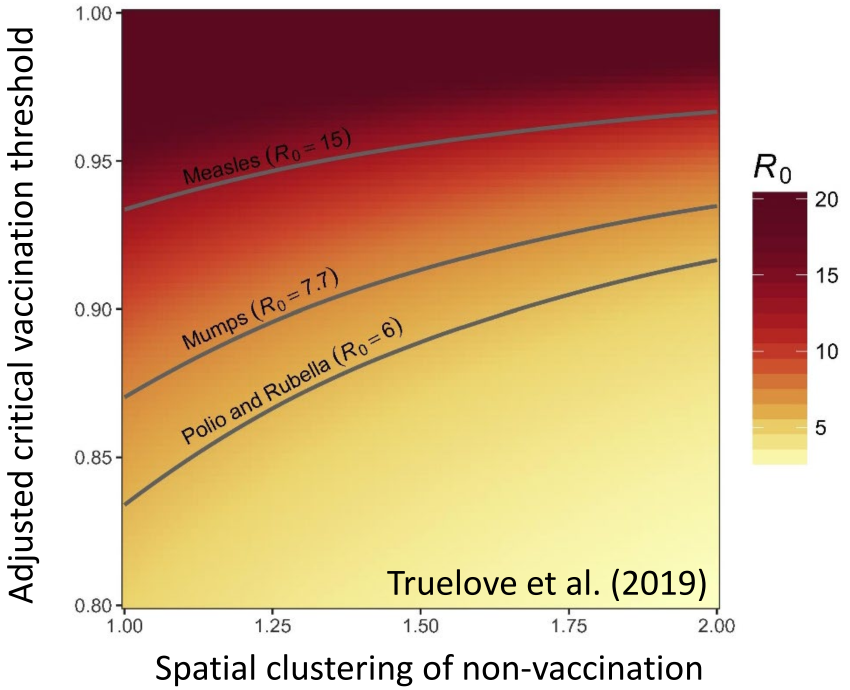
Spatial clustering of non-vaccinated individuals can increase required vaccination rates to avoid large outbreak

Visualization of spatial clustering of non-vaccinated individuals



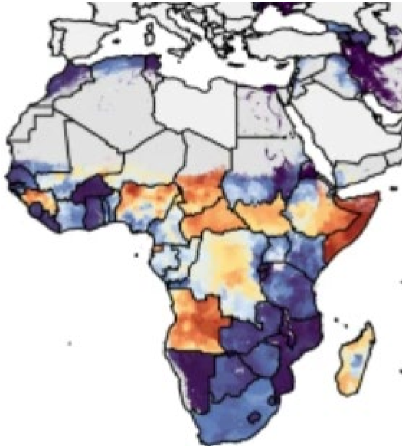
Truelove et al. (2019)

Impact of spatial clustering on vaccination coverage necessary to avoid outbreaks

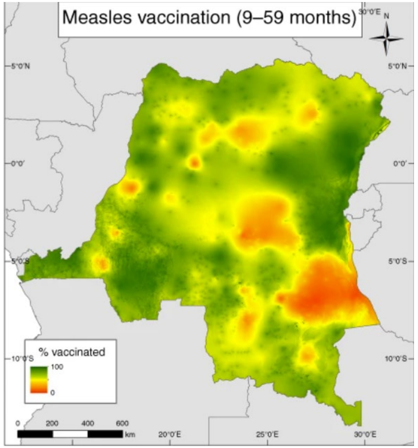


How can we create spatial distributions of vaccination coverage for our simulations?

MCV Vaccination

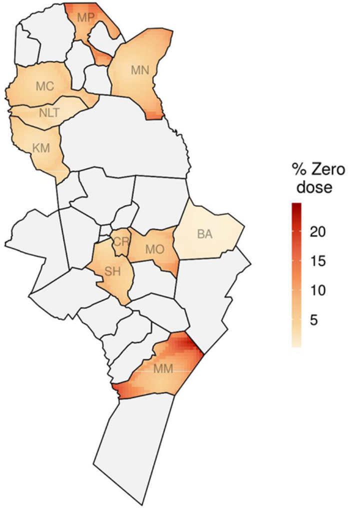


Sbarra et al. (2020)

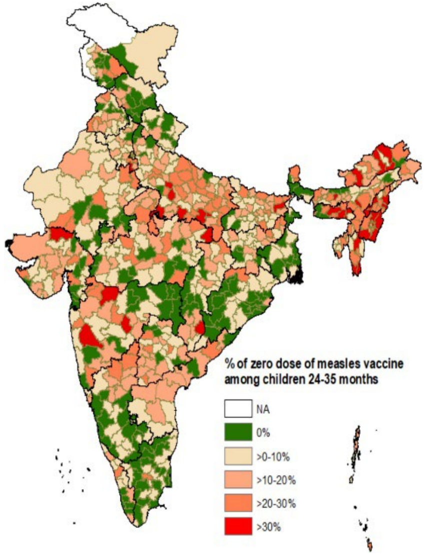


Utazi et al (2019)

Zero dose (MCV)



Arambepola et al. (2021)



Dhalaria et al. (2024)

 |

References

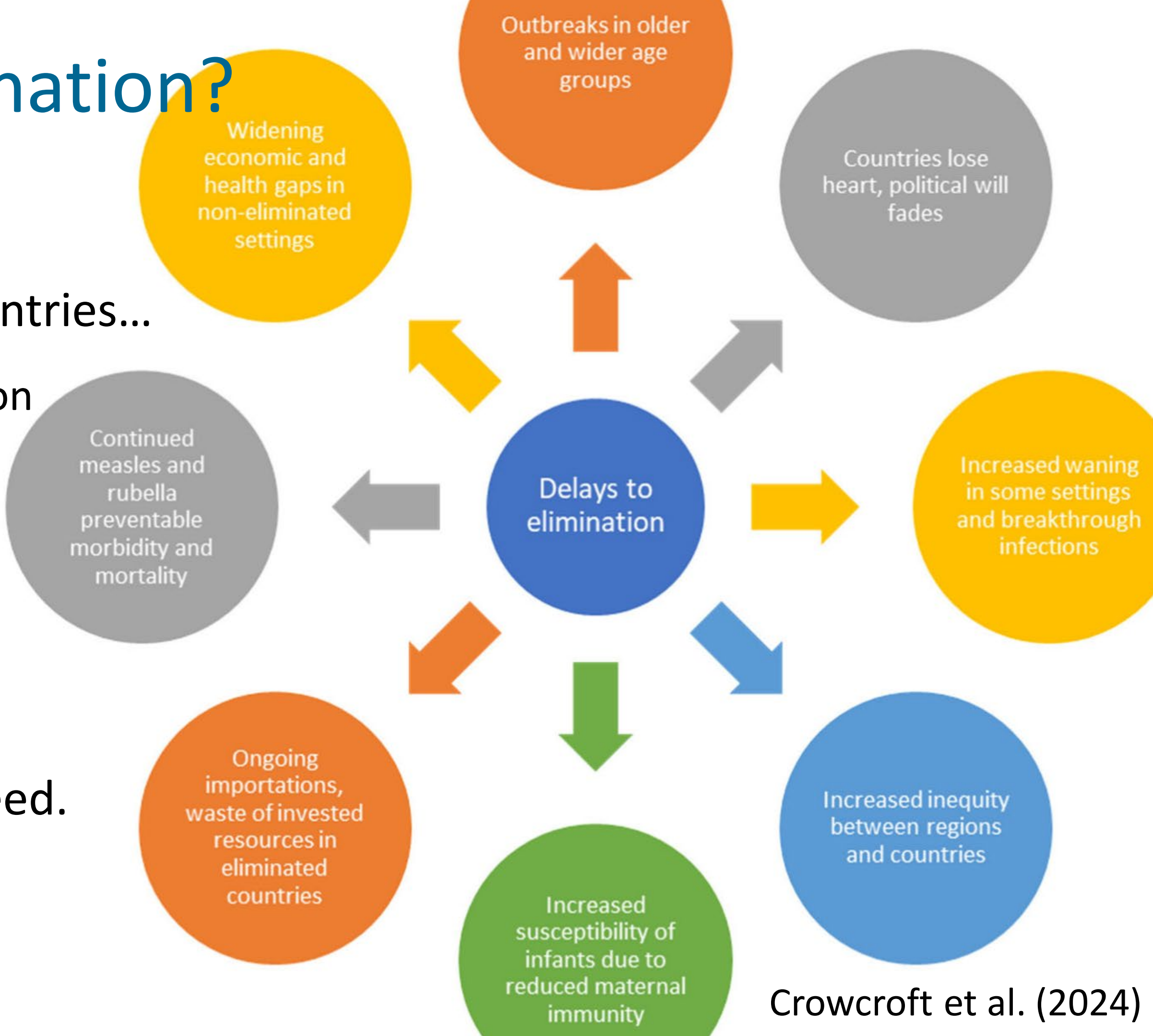
- Accelerating measles elimination in the Western Pacific Region during the calm between the storms

Why measles elimination? Why now?

Delay elimination in some countries…

- Increasing inequity in vaccination coverage means outbreaks are more likely and larger
- Difficult to sustain political will
- Waning immunity may re-establish transmission

makes it harder for all to succeed.



Crowcroft et al. (2024)

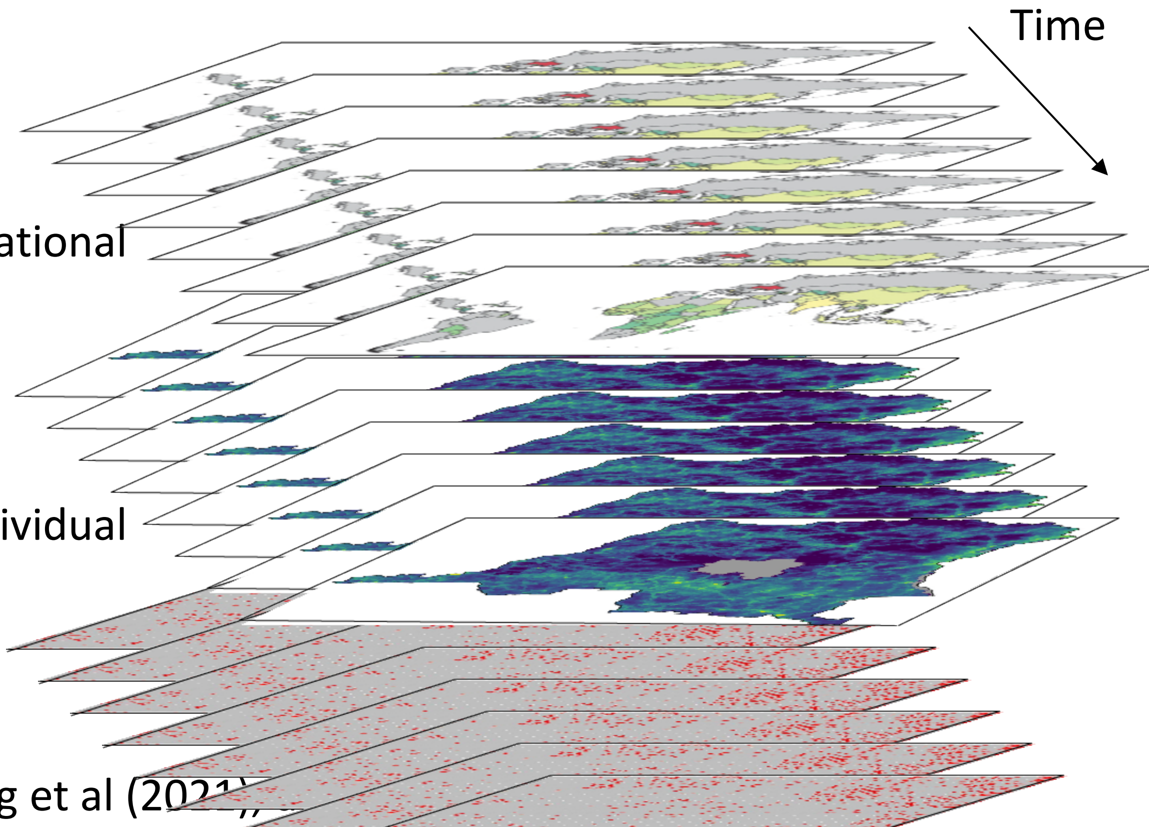
We require high spatial and individual resolution

Global, Continental, National

We want to model individual agents on multi-national scales, but space is not the only one…

Subnational

Individual



Figures from Winter et al (2022), Cheng et al (2021), …

Related work on importations?

Relative risk of importations by state and month